

PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Urinary tract infections in children- an overview of diagnosis and management
AUTHORS	Kaufman, Jonathan; Temple-Smith, Meredith; Sanci, Lena

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Morris Gordon Institution and Country: UCLAN, UK Competing interests: ASSOCIATE EDITOR OF JOURNAL
REVIEW RETURNED	13-Aug-2019

GENERAL COMMENTS	<p>I think this is a great topic for review, reads well and is essentially correct. However, I feel it represents a lost opportunity. Much of the content is already represented in the key guidance from the UK / USA / Australia that are cited.</p> <p>Therefore, what the paper needs to do is highlight the areas of convergence and divergence in key pragmatic decision points and perhaps do this using a slightly wider net that currently. This could easily be added</p> <p>For example, for imaging advice, I am very familiar with this in the UK - what other countries are aligned - specifically, what countries are not aligned and if not, is there a rationale.</p> <p>Similarly, for diagnosis, acute management. This small amendment will make this a far more pragmatic and international piece, whilst not losing its current great strengths and I hope you will be able to revise.</p>
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REVIEWER	Reviewer name: Krishna Kishore Umapathi Institution and Country: Rush University Medical Center, USA Competing interests: None
REVIEW RETURNED	03-Sep-2019

GENERAL COMMENTS	<p>This is a comprehensive review by Kaufman et al on the topic "Urinary Tract Infections in Children" where they have attempted to focus on the recent updates on diagnostics and treatment. Overall, the article covers most of the aspects associated with UTI in children and the lack of evidence in certain aspects of management. Please see below for a few minor grammatical revisions</p> <p>1. BACKGROUND:</p> <p>Prevalence and epidemiology Line 38 - Change "further UTI" to recurrent UTI. Line 46 - Change As such a common infection to - Being such a common infection</p>
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	<p>Aetiology</p> <p>1. It would be better to insert a small table or a figure showing relative prevalence of each microorganism that causes UTI instead of just mentioning E.Coli. This might be done by stratifying age as each population is different in terms of risk factors</p> <p>2. The etiology might be different based on patient characteristics. eg: hospital acquired UTI are more commonly Enterococcus. A sentence mentioning the same would be apt in this section.</p> <p>Morbidity:</p> <p>1. Third paragraph: change to - "as this population".</p> <p>2. No need for a third paragraph, can be joined with second as they both talk about short term morbidity</p> <p>DIAGNOSIS</p> <p>Urine Sample Collection: precontinent children</p> <p>Line 10 - Remove the use of Most repeatedly in the sentence</p> <p>Line 59 - Change to - but therapy should not be delayed in a septic child</p> <p>Screening -dipstick and microscopy</p> <p>Please mention which uropathogens dont convert nitrates to nitrites. This is important clue for diagnosing enterococcus for example until cultures come back</p> <p>INITIAL MANAGEMENT</p> <p>Antibiotic therapy:</p> <p>Line 46 - Expand NICE</p> <p>Line 55 - Change to " It is ideal to switch to oral therapy after 48 hours of clinical improvement to facilitate homegoing or discharge"</p> <p>There is no mention of any antibiotics that are commonly used for UTI. A paragraph can be inserted mentioning the same.</p> <p>SPECIAL CASES</p> <p>Recurrent UTI: prophylaxis and prevention</p> <p>There is no mention on choice of antibiotic prophylaxis if indicated</p> <p>Is there a role for probiotics? If so or not so, please add references</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1

I think this is a great topic for review, reads well and is essentially correct. However, I feel it represents a lost opportunity. Much of the content is already represented in the key guidance from the UK / USA / Australia that are cited. Therefore, what the paper needs to do is highlight the areas of convergence and divergence in key pragmatic decision points and perhaps do this using a slightly wider net that currently. This could easily be added For example, for imaging advice, I am very familiar with this in the UK - what other countries are aligned - specifically, what countries are not aligned and if not, is there a rationale. Similarly, for diagnosis, acute management. This small amendment will make this a far more pragmatic and international piece, whilst not loosing its current great strengths

□ thank you, we have incorporated this helpful suggestion and discussed further under ultrasound recommendations and amended Table 2 to include other guidelines as well as NICE and AAP. Additional references are included as well. This suggested comparison is also included in the section regarding urine sample collection in young pre-continent children, with additional recently published cost-effectiveness data. Other guidelines are now also discussed and referenced regarding antibiotic therapy.

Reviewer 2

This is a comprehensive review by Kaufman et al on the topic "Urinary Tract Infections in Children" where they have attempted to focus on the recent updates on diagnostics and treatment. Overall, the article covers most of the aspects associated with UTI in children and the lack of evidence in certain aspects of management. Please see below for a few minor grammatical revisions

1. BACKGROUND:

Prevalence and epidemiology

Line 38 - Change "further UTI" to recurrent UTI.

□ amended as suggested

Line 46 - Change As such a common infection to - Being such a common infection

□ amended as suggested

Aetiology

1. It would be better to insert a small table or a figure showing relative prevalence of each microorganism that causes UTI instead of just mentioning E.Coli. This might be done by stratifying age as each population is different in terms of risk factors

2. The etiology might be different based on patient characteristics. eg: hospital acquired UTI are more commonly Enterococcus. A sentence mentioning the same would be apt in this section.

□ as exact uropathogen prevalence varies between settings and between studies (beyond E.Coli as the overwhelmingly predominant organism in all settings), we feel this would be difficult to summarise concisely for an international audience. We have however considered this suggestion and thought that from a clinical perspective it would be helpful for readers to be aware that Enterococcus and Klebsiella UTI may be missed on dipstick screening because these organisms do not produce nitrites, and also are less likely to present with pyuria than E.Coli UTI. We have therefore included later in the manuscript under 'Screening – dipstick and microscopy' the following:

“Enterococcus, Klebsiella and Pseudomonas species are less likely to produce pyuria than E.coli in children with symptomatic UTI. 26 Most uropathogens convert dietary nitrates into urinary nitrites. However not all do, including Enterococcus and Klebsiella species. 25”

Morbidity:

1. Third paragraph: change to - "as this population".

☐ amended as suggested

2. No need for a third paragraph, can be joined with second as they both talk about short term morbidity

☐ amended as suggested

DIAGNOSIS

Urine Sample Collection: precontinent children

Line 10 - Remove the use of Most repeatedly in the sentence

☐ amended as suggested

Line 59 - Change to - but therapy should not be delayed in a septic child

☐ amended as suggested

Screening -dipstick and microscopy

Please mention which uropathogens dont convert nitrates to nitrites. This is important clue for diagnosing enterococcus for example until cultures come back

☐ amended as suggested

INITIAL MANAGEMENT

Antibiotic therapy:

Line 46 - Expand NICE

☐ amended as suggested

Line 55 - Change to " It is ideal to switch to oral therapy after 48 hours of clinical

improvement to facilitate homegoing or discharge"

There is no mention of any antibiotics that are commonly used for UTI. A paragraph can be inserted mentioning the same.

□ As the journal has an international readership, and there is such significant variation in empiric therapy between regions, we agree this is an important point but feel it would be difficult to elaborate in a meaningful way within the wordcount available. It is mentioned in the preceding paragraph, "Choice of empiric antibiotics must be guided by local guidelines, as local antimicrobial sensitivities vary significantly (Table 3)."

SPECIAL CASES

Recurrent UTI: prophylaxis and prevention

There is no mention on choice of antibiotic prophylaxis if indicated

□ as for initial management, as this should be informed by local antimicrobial sensitivities, we have specifically avoided suggesting a particular antibiotic agent

Is there a role for probiotics? If so or not so, please add references

□ amended as suggested, referenced to recent Cochrane review